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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/822,423	04/12/2004	Stephen P.A. Fodor	3594.1	2561

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EXAMINER	
LIU, SUE XU	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 12/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/822,423	FODOR, STEPHEN P.A.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/9/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *8 and 12-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (Claims 1-11) in the reply filed on 11/9/2005 is acknowledged.

2. Claims 12-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/9/2005.

3. Applicants also elected the following species:

A.) 2 different labels;

B.) Beads as support;

C.) Simultaneous hybridization;

D.) Microarray.

Accordingly, Claim 8 is withdrawn due to non-elected species.

4. Claims 1-22 are currently pending;

Claims 8 and 12-22 have been withdrawn;

Claims 1-7 and 9-11 are being examined in this application.

Priority

5. This application claims priority to provisional application 60/462,508 filed on 04/11/2003.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-7 and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 of the instant application recite a method for analyzing a nucleic acid sample by using different nucleic acid affinity matrices and labels. The steps of the methods are not clearly defined. For example, the step of "labeling of the first and second sets of nucleic acids with different labels" could be carried out before the hybridization step. How is each set of nucleic acid labeled differentially with different labels when they are in the same sample? In addition, it is also not clear whether the "collections of beads" recited in Claim 3 are the same bead array directed in Claim 11. Therefore, the instant claims failed to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1-7 and 9-11 are rejected under **35 U.S.C. 102(b)** as being anticipated by Fodor et al (US 5,800,992; 09/01/1998).

The instant claims briefly recite a method comprising hybridizing two different sets of nucleic acids with two different nucleic acid affinity matrices (which consist of nucleic acids attached to beads microarrays); labeling the two sets of nucleic acids with different fluorescent labels; detecting the two different sets of nucleic acids.

Fodor et al teach a method of detecting nucleic acid sequences in two or more collections of nucleic acid molecules (would read on two different sets (first and second sets) of nucleic acids; See Claim 1 of the reference, for example). The reference teaches "contacting" or hybridizing the "first collection of labeled nucleic acid" and "at least a second collection of labeled nucleic acid" to an array of polynucleotides (would read on oligonucleotide probes) bound to a solid surface (See Claim 1 of the reference). This would read on hybridizing the first and second sets of nucleic acids to two different nucleic acid affinity matrices since the an array of polynucleotides would contain complementary nucleic acids to the different sets of nucleic acids. The reference further teaches that the first and second labels are distinguishable from each other (see Claim 1 of the reference), and the labels are fluorescent labels with different emission colors (Claims 3 and 4 of the reference). This would read on different fluorescent labels having different colors. Furthermore, the reference teaches the solid support comprises an array of beads (referring to "collections of beads, microarray and bead array; See Claim 2 of the reference), and detecting hybridization of the first and second labeled complementary nucleic acids to nucleic acids of the array (would refer to detection comprising hybridizing the labeled first and second sets of the nucleic acids; See Claim 1 of the reference). Additionally, the

reference teaches "adding a mixture of labeled nucleic acids from the two cell types to an array..." which would read on mixing the first and second sets of nucleic acids before simultaneous hybridization (See Claim 4 of the reference).

Thus the reference clearly anticipates the claimed invention.

10. Claims 1, 2, 4-7, 9 and 10 are rejected under **35 U.S.C. 102(b)** as being anticipated by Fodor et al (US 6,309,822 B1; 10/30/2001).

The instant claims briefly recite a method comprising hybridizing two different sets of nucleic acids with two different nucleic acid affinity matrices (which consist of nucleic acids attached to beads microarrays); labeling the two sets of nucleic acids with different fluorescent labels; detecting the two different sets of nucleic acids.

Fodor et al teach a method for comparing and identifying differences in nucleic acid sequences in two or more collections of labeled nucleic acids (See Claim 1). The reference teaches providing a plurality of probes (comprises complementary nucleic acids) bound to a solid surface (would refer to first and second nucleic acid affinity matrices; See Claim 1). The reference also teaches contacting the probes with a first and second collection of labeled nucleic acids and detecting the binding of the labeled nucleic acids (Claim 1), which would refer to detecting the first and second sets of nucleic acids. The reference further teaches the first and second labels are fluorescent labels with different colors (See Claims 2-4). In addition, the reference teaches mixing labeled DNA samples from two different cell types (diseased and normal), and contacting them simultaneously with probes on a microarray (See paragraph [720] of the reference).

Thus the reference clearly anticipates the claimed invention.

11. Claims 1-7 and 9-11 are rejected under **35 U.S.C. 102(e)** as being anticipated by Fodor et al (US 6,576,424 B2; 06/10/2003; Filed 1/25/2001).

The instant claims briefly recite a method comprising hybridizing two different sets of nucleic acids with two different nucleic acid affinity matrices (which consist of nucleic acids attached to beads microarrays); labeling the two sets of nucleic acids with different fluorescent labels; detecting the two different sets of nucleic acids.

Fodor et al teach a method of detecting nucleic acid sequences in two or more collections of nucleic acid molecules (would read on two different sets (first and second sets) of nucleic acids; See Claims 17 and 43 of the reference, for example). The reference teaches "contacting" or hybridizing the "first collection of labeled nucleic acid" and "at least a second collection of labeled nucleic acid" to an array of polynucleotides (would read on oligonucleotide probes) bound to solid substrates (e.g. Claims 1, 17 and 43 of the reference). This would read on hybridizing the first and second sets of nucleic acids to two different nucleic acid affinity matrices since the an array of polynucleotides would contain complementary nucleic acids to the different sets of nucleic acids. The reference further teaches that the first and second labels are distinguishable from each other (e.g. Claims 17 and 43 of the reference), and the labels are fluorescent labels with different emission colors (e.g Claim 60 of the reference). This would read on different fluorescent labels having different colors. Furthermore, the reference teaches the solid support comprises an array of beads (referring to "collections of beads, microarray and bead array; See Claim 44 of the reference), and detecting hybridization of the first and second

labeled complementary nucleic acids to nucleic acids of the array (would refer to detection comprising hybridizing the labeled first and second sets of the nucleic acids; See Claim 17 of the reference). Additionally, the reference teaches "adding fluorescent labeled nucleic acids from the two cells to an array..." which would read on mixing the first and second sets of nucleic acids before simultaneous hybridization (See Claim 60 of the reference).

Thus the reference clearly anticipates the claimed invention.

12. Claims 1, 2, 4-7, 9 and 10 are rejected under **35 U.S.C. 102(e)** as being anticipated by Fodor et al (US 6,551,784 B2; 4/22/2003; Filed 5/9/2001).

The instant claims briefly recite a method comprising hybridizing two different sets of nucleic acids with two different nucleic acid affinity matrices (which consist of nucleic acids attached to beads microarrays); labeling the two sets of nucleic acids with different fluorescent labels; detecting the two different sets of nucleic acids.

Fodor et al teach a method for identifying differences in nucleic acid sequences in two or more collections of labeled nucleic acids (See Claim 1). The reference teaches providing a plurality of probes (comprises complementary nucleic acids) bound to a solid surface (would refer to first and second nucleic acid affinity matrices; See Claim 1). The reference also teaches contacting the probes with a first and second collection of labeled nucleic acids and detecting the binding of the labeled nucleic acids (Claim 1), which would refer to detecting the first and second sets of nucleic acids. The reference further teaches the first and second labels are fluorescent labels with different colors (See Claims 2-4). In addition, the reference teaches

mixing labeled DNA samples from two different cell types (diseased and normal), and contacting them simultaneously with probes on a microarray (See paragraph [604] of the reference).

Thus the reference clearly anticipates the claimed invention.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-7 and 9-11 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Lichtenwalter (US 5,683,875; 11/04/1997), in view of Fodor et al (US 5,800,992; 09/01/1998).

The instant claims briefly recite a method comprising hybridizing two different sets of nucleic acids with two different nucleic acid affinity matrices (which consist of nucleic acids attached to beads microarrays); labeling the two sets of nucleic acids with different fluorescent labels; detecting the two different sets of nucleic acids.

Lichtenwalter teaches a method for detecting a target nucleic acid analyte in a sample using immobilized capture oligonucleotide (See Abstract). The reference teaches a capture oligonucleotide attached to substrate (magnetically responsive particles, which would refer to beads and nucleic acid matrices.). (See Claim 1 of the reference) The reference also teaches hybridizing the capture oligonucleotide with the nucleic acid analyte (referring to nucleic acid samples). (Claim 1) The reference further teaches detecting the capture oligonucleotide-analyte complex with a detectable labeled analyte-bindng molecule (Claim 1), which would refer to the

detection step in the instant claims. In addition, the reference teaches that the detectable label is a fluorescer as well as a plurality of fluorescers (which would refer to the different fluorescent labels; See Claims 3 and 4).

Lichtenwalter does not teach two different sets of nucleic acid samples or two different sets of nucleic acid affinity matrices. The reference also does not specifically teach the different fluorescent labels have different colors. The reference also does not teach the using a microarray as well as simultaneous hybridization.

However, Fodor et al teaches a method of detecting nucleic acid sequences in two or more collections of nucleic acid molecules as described supra. Fodor et al also teaches the advantages of detecting two sets of nucleic acid samples with two sets of nucleic acid affinity matrices such as the possibility for high resolution testing of many different interactions simultaneously (See Paragraph [256] of the reference).

Therefore, it would have been prima facie obvious for an ordinary skilled artisan to generate a method for detecting different nucleic acid samples with different nucleic acid probes attached to solid substrate (such as beads) by using distinguishable fluorescent labels. Due to the advantages taught by Fodor et al, a person of ordinary skill in the art would have been motivated at the time of the invention to modify the method taught by Lichtenwalter by generating two different probe sets and using two different nucleic acid samples. Since all the necessary techniques for detecting nucleic acid using immobilized probes (including generating immobilized nucleic acid probes; preparing nucleic acid samples; nucleic acid hybridization; nucleic acid labeling with fluorescent labels; detecting fluorescent labels; using microarray for detecting nucleic acid hybridization) are known in the art as taught by Lichtenwalter and Fodor

et al, a person of ordinary skill in the art would have reasonable expectation of success of achieving detecting two sets of nucleic acid samples simultaneously with two different probe sets.

In conclusion, the invention of the instant claims would have been prima facie obvious over Lichtenwalter, in view of Fodor et al to one of ordinary skill in the art without evidence to the contrary.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1-7 and 9-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 5,800,992 (henceforward referred to as '992 patent). Although the conflicting claims are not identical, they are not

patentably distinct from each other because the scope of the invention as recited in the instant application's claims would read on the scope of '992 patent claims or vice versa. The '992 patent claims a method of detecting nucleic acid sequences in two or more collections of nucleic acid molecules (would read on two different sets (first and second sets) of nucleic acids; See Claim 1 of '992, for example). The patent teaches "contacting" or hybridizing the "first collection of labeled nucleic acid" and "at least a second collection of labeled nucleic acid" to an array of polynucleotides (would read on oligonucleotide probes) bound to a solid surface (See Claim 1 of '992). This would read on hybridizing the first and second sets of nucleic acids to two different nucleic acid affinity matrices since the an array of polynucleotides would contain complementary nucleic acids to the different sets of nucleic acids. The patent further teaches that the first and second labels are distinguishable from each other (see Claim 1), and the labels are fluorescent labels with different emission colors (Claims 3 and 4 of '992). This would read on different fluorescent labels having different colors. Furthermore, the patent teaches the solid support comprises an array of beads (referring to "collections of beads, microarray and bead array; See Claim 2 of '992), and detecting hybridization of the first and second labeled complementary nucleic acids to nucleic acids of the array (would refer to detection comprising hybridizing the labeled first and second sets of the nucleic acids; See Claim 1 of '992). Additionally, the patent teaches "adding a mixture of labeled nucleic acids from the two cell types to an array..." which would read on mixing the first and second sets of nucleic acids before simultaneous hybridization (See Claim 4 of '992).

17. Claims 1, 2, and 4-7 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,309,822 B1 (henceforward referred to as '882 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the invention as recited in the instant application's claims would read on the scope of '882 patent claims or vice versa. The '882 patent teaches a method for comparing and identifying differences in nucleic acid sequences in two or more collections of labeled nucleic acids (See Claim 1). The patent teaches providing a plurality of probes (comprises complementary nucleic acids) bound to a solid surface (would refer to first and second nucleic acid affinity matrices; See Claim 1). The patent also teaches contacting the probes with a first and second collection of labeled nucleic acids and detecting the binding of the labeled nucleic acids (Claim 1), which would refer to detecting the first and second sets of nucleic acids. The patent further teaches the first and second labels are fluorescent labels with different colors (See Claims 2-4).

18. Claims 1-7 and 9-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16, 17 and 39-64 of U.S. Patent No. 6,576,424 B2 (henceforward referred to as '424 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the invention as recited in the instant application's claims would read on the scope of '424 patent claims or vice versa. The '424 patent teaches a method of detecting nucleic acid sequences in two or more collections of nucleic acid molecules (would read on two different sets (first and second sets) of nucleic acids; See Claims 17 and 43 of '424, for example). The patent teaches "contacting" or hybridizing the

"first collection of labeled nucleic acid" and "at least a second collection of labeled nucleic acid" to an array of polynucleotides (would read on oligonucleotide probes) bound to solid substrates (e.g. Claims 1, 17 and 43 of '424). This would read on hybridizing the first and second sets of nucleic acids to two different nucleic acid affinity matrices since the an array of polynucleotides would contain complementary nucleic acids to the different sets of nucleic acids. The patent further teaches that the first and second labels are distinguishable from each other (e.g. Claims 17 and 43 of '424), and the labels are fluorescent labels with different emission colors (e.g Claim 60 of '424). This would read on different fluorescent labels having different colors. Furthermore, the reference teaches the solid support comprises an array of beads (referring to "collections of beads, microarray and bead array; See Claim 44 of '424), and detecting hybridization of the first and second labeled complementary nucleic acids to nucleic acids of the array (would refer to detection comprising hybridizing the labeled first and second sets of the nucleic acids; See Claim 17 of '424). Additionally, the patent teaches "adding fluorescent labeled nucleic acids from the two cells to an array..." which would read on mixing the first and second sets of nucleic acids before simultaneous hybridization (See Claim 60 of '424).

19. Claims 1, 2, and 4-7 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 and 20 of U.S. Patent No. 6,551,784 B2 (henceforward referred to as '784 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the invention as recited in the instant application's claims would read on the scope of '784 patent claims or vice versa. The '784 patent teaches a method for identifying differences in nucleic acid sequences in two or more

collections of labeled nucleic acids (See Claim 1 of '784). The reference teaches providing a plurality of probes (comprises complementary nucleic acids) bound to a solid surface (would refer to first and second nucleic acid affinity matrices; See Claim 1). The reference also teaches contacting the probes with a first and second collection of labeled nucleic acids and detecting the binding of the labeled nucleic acids (Claim 1), which would refer to detecting the first and second sets of nucleic acids. The reference further teaches the first and second labels are fluorescent labels with different colors (See Claims 2-4).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL
Art Unit 1639
12/1/2005

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PRIMARY EXAMINER